REMARKS

Claims 1-19, 21-35 and 39-57 are pending in the subject application. Claims 1-3 have been amended. The amendments to claims 1-3 is supported by the specification as filed, and no new matter is presented. Favorable reconsideration in light of the remarks which follow is respectfully requested.

1. 35 U.S.C. §103 Rejections

Claims 1-4, 12-16, 19, 21-23 and 25-33

Claims 1-4, 12-16, 19, 21-23 and 25-33 have been rejected under 35 U.S.C. §103(a) as being unpatentable over Le et al (US Pat#6,355,027) in view of applicant's own disclosure. The Office asserts that:

> Le discloses a flexible microcatheter system having a flexible cannula (16) with a proximal end and a distal end. The system also has a second cannula (14) having a larger diameter than the flexible cannula and is less flexible (l:46-49). The second cannula has a proximal end and a distal end and a portion of the flexible cannula is housed within the distal end of the second cannula (see figures 1-3). The second cannula forms a fluid tight seal and mounted about the flexible cannula (see figure 3; the mounting of cannula 14 and 16 within proximal connector 12 must be fluid tight between all three components in order to prevent leaking). The proximal end of the second cannula is sized for attachment (connector 12) to the tip of a syringe.
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> Regarding the function language in claims 1-4, 16, 25-33 that generally provide for the functioning of the microcatheter or cannula as a hands free injection system. The examiner reminds applicant that function language in device claims is given little patentable weight. As long as the prior art device meets the structural limitations of the claims and is capable of performing the claimed function then the prior art reads on the claims.
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> In the claims above, the instant invention is a device that injects into the retinal vein of the eye for periods of time from at least 5 min to 2 hours using no support systems to hold the device in position and provides an infusion flow rate of 0.2 cc/min through the proximal end of the second cannula. The prior art is capable of performing this function due to the fact that it is a microcatehter for use in small and tortuous vascular paths and is made from flexible materials.
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> Additionally, while Le fails to disclose a modified microcannula system having a silicone plug with a central aperture applicant's own disclosure renders this limitation obvious. Page 10 of the instant application states that "microcannula are well known" an "the general features...may be in accordance with conventional catheters". Furthermore, silicone plugs with central apertures (otherwise known in the art as hemostatic valves) are well known in the cannula art and are

used for maintaining bodily fluids within the body when a larger cannula punctures the body and another instrument is inserted through the larger cannula.

Applicants respectfully traverse.

Le describes a flexible microcatheter that has regions of varying flexibility along the length of a one-piece composite catheter tube 16. In particular, the catheter tube 16 has a distal region of flexibility 20, a mid region of flexibility 22 and a proximal region of flexibility 24. The degree of flexibility decreases towards the catheter proximal end. The microcatheter further includes a strain relief 14 and a Luer connector 16, wherein the catheter tube 16 is connected to the Luer connector 16 via the strain relief 14.

As set out by Le, prior catheters for use in small and tortuous vascular paths required catheters of minimal profile and a great degree of flexibility. However, a catheter of minimal profile may be too flexible such that the catheter will kink in a tight radius path. Further, such devices will frequently not possess the required structural integrity required to advance the catheter along a path or to twist the catheter along the path, which resulted in kinking of the catheter at various points along the catheter length. (See col. 1, lines 13-25)

In particular, the types of microcatheter described by Le are those designed for procedures wherein the catheter tip is inserted into a vascular path and the length of the catheter is pushed up through the vascular path to a target location by pushing the catheter from its proximal end. On common type of procedure wherein the microcatheter of Le is used is, for example, the treatment of heart conditions (e.g. atrial fibrillation). For the treatment of heart conditions using the catheter system, an incision is generally made in the patient's upper thigh and the catheter is inserted through a blood vessel in the upper thigh and is pushed all the way up to the heart. Thus, in this type of a procedure, the catheter must travel from the thigh area all the way up to the heart by being pushed and directed through a blood vessel running from the thigh to the heart.

Such procedures require catheters of substantial length. Thus, as set out by Le, the length of the catheter tube 16 measured from the strain relief to the tip can range from 100 to 160 cm (39 – 63 inches). Further, the catheter must possess some degree of flexibility along its length to allow for the catheter to be directed along pathways that are curved. However, the catheter must not be so flexible that it cannot be pushed from its proximal end through such a pathway. In particular, the microcatheter of Le is specifically designed for insertion into lengthy vascular pathways and it must be flexible, but not too flexible such that it would bend or kink when pushed through a vascular pathway from its proximal end (col. 1, lines 13-25).

Applicants, on the other hand, teach a very different type of microcatheter system for infusion of a solution into a retinal vein. Applicants' microcatheter system is designed such that it is capable of remaining within the retinal vein during the infusion without an external holding device for at least a period of time required for a bolus injection. The microcatheter system includes a modified microcannula system wherein a flexible cannula is mounted in or is at least partially encased in a second cannula (claims 1-3). Further, the flexible cannula preferably has a sharp distal tip for puncturing the retinal vein lumen (claim 1)

In Figs. 4-8, Applicants' microcatheter system is shown as it is inserted into the eye directly in-line with the retinal vein to be cannulated. The distal tip of the flexible cannula 2 is advanced to the retinal vein and inserted to allow for the infusion of solution into the retinal vein. In particular, Applicants' flexible cannula is designed to be grasped at the tip and inserted into the retinal vein once it is inside the body. Applicants' cannula is not pushed from the proximal end nor is it advanced along its length through the pathway of the retinal vein like Le's device. Rather, Applicants' cannula 2 is inserted into the retinal vein an amount sufficient for it to be secure in the retinal vein and to prevent unwanted dislodgement as a solution is infused through the cannula into the vein. Further, Applicants' flexible cannula has means (e.g. tabs or wings) to prevent it from being crushed when the surgeon grasps the tip. These tabs or wings also allow the cannula to be positioned parallel to the retinal vein and as close as possible to the retinal vein prior to insertion without the grasping device interfering. Tabs or wings on the Le device, on the other hand, would interfere

with use of the Le device as the device is pushed from itsa proximal end and must traverse long distances inside a tortuous pathway.

Thus, while the Le microcatheter is designed for insertion and advancement along its length through a vascular pathway by pushing the microcatheter from its proximal end, Applicants' microcatheter is designed such that the distal end of the flexible cannula is inserted into a retinal vein.

Thus, Applicants respectfully submit that the microcatheter of Le is a very different type of microcatheter than that taught by Applicants.

Applicants found, in particular, that prior microcannula designed for extended infusion into retinal veins (longer than bolus injection) presented many problems. For example, it was necessary to use rigid cannula held in place by hand or by use of a robot or a micromanipulator, which provide a mechanical aid to keep the instrument in place during and after the retinal venous puncture. In any event, even using these holding means, human tremor and involuntary motions make it extremely difficult to prevent dislodgement of the cannula. Further, it was often required to fix the head and eye of the patient by using eye rings, sutures, head straps, and other such physical restraints to further prevent dislodgement. However, even with such methods, a micron scale motion of either the patient, the micropipette, the manipulator or the surgeon may cause the cannula to be dislodged.

Thus, Applicants solved these problems by providing a microcatheter designed specifically for insertion into a retinal vein and prolonged infusion of solutions into the retinal vein without the need for external holding devices. In particular, Applicants' microcatheter system is designed to include a flexible cannula and a second cannula, wherein the flexibility of the first cannula is such that it prevents the cannula from being dislodged from the retinal vein and allows for the cannula to remain within the retinal vein during the infusion without an external holding device for at least a period of time required for a bolus injection.

Thus, the Le microcatheter is designed for insertion and advancement through a tortuous pathway. As such, is designed with a variable flexibility along its length to allow for advancement through the pathway. The catheter is pushed from its proximal end through the pathway and, thus, the catheter is designed with less flexibility toward its distal end and more flexibility toward its proximal end. In any event, the catheter must not be too flexible along its length such that the catheter will bend or kink when advanced through a tortuous pathway (i.e. with curves). Applicants' microcatheter, on the other hand, is designed for insertion into a patient's eye and into a retinal vein and is designed to have flexibility that allows it to remain within the retinal vein without external holding devices. As noted above, very minor movements by the patient and/or surgeon can dislodge the microcatheter from a retinal vein. Thus, Applicants' microcatheters are designed with a flexibility that will overcome any movement that would cause dislodgement.

Applicants respectfully submit that the microcatheters of Le would not be capable of performing Applicants' claimed function for a number of reasons. Le's device is designed for a very different use and, as such, it is designed with different properties. The flexibility required of the Le device is different than that required of Applicants' device. Further, the varying degrees of flexibility along the length of Le's microcatheter may prevent the device from performing Applicants' claimed function. As set out by Le, "A further significant aspect and feature of the present invention is a flexible microcatheter having a relatively stiff proximal region for application of push force to the distal flexible region(s)." (Col. 2, lines 8-12) Applicants respectfully submit that having a relatively stiff proximal region would likely result in dislodgement of the catheter from the retinal vein. Retinal veins are very small (approximately 100 μm in diameter). If the catheter tip is inside the retinal vein in accordance with Applicants' invention, even if it is in the middle of the retinal vein, a movement as small as 50 μm can cause the tip of the catheter to be pushed through and out of the vein. Thus, Applicants' catheters must be very flexible along their lengths so that any movement is absorbed by the flexibility of the catheter. Further, Le is specifically designed with a flexibility that is limited to prevent bending and kinking along the catheter length as it is pushed through a curved pathway. Applicants respectfully

submit that such a flexibility would be insufficient to absorb the movements that could dislodge Applicants' microcatheter from micron sized retinal veins.

Further, regarding the Office's assertion that "Le discloses a flexible microcatheter system having a flexible cannula (16) with a proximal end and a distal end. The system also has a second cannula (14) having a larger diameter than the flexible cannula and is less flexible (l:46-49)," Applicants respectfully submit that Le describes a catheter tube 16 and a strain relief 14, not a second cannula. It is common to employ various types of strain relief mechanisms in cannulas like that described by Le for insertion into and through vascular paths. These strain relief mechanisms serve as adjunctive components designed to relieve stress from a functional component of a device and designed to reinforce the catheter in the area where the user applies force on the catheter. The strain relief of Le is not a second cannula in accordance with Applicants' teaching. Applicants' second cannula is a functioning part of the fluid delivery portion of Applicants' microcannula system wherein the inner diameter of the second cannula transfers the solution to the flexible cannula and into the retinal vein. Further, according to Applicant,

> * * *the intraocular part of the microcatheter system is composed of a hybrid of two different size cannulae 2, 14. In addition to the above-described cannula 2 that is inserted into the retinal vein lumen, the microcatheter system further comprises a larger cannula 14 that encases a portion of the cannula 2.
>
> In a preferred embodiment, the larger cannula 14 forms the part of the microcatheter system that is placed just inside the eye. The larger cannula 14 provides the rigidity necessary to pass it into the eye without damage and is less flexible than the smaller cannula 2.* * * (page 14, lines 12-26)

As such, the strain relief 14 of Le would not be a second cannula in accordance with Applicants' disclosure. Le's strain relief is merely a portion of the device that joins the luer connector to the catheter tube and is formed so as to relieve stress and reinforce the catheter in the area where the user applies force on the catheter. Further, as set forth above, Le's catheter tube 16 ("flexible cannula) extends about 3-6 feet in length from the end of the strain relief 14. Thus, the strain relief 14 would not be an intraocular part of the microcatheter and would not be placed inside the eye.

To establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, and not based on applicant's disclosure. *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991). MPEP 2142.

Le does not teach or suggest all the claim limitations. As set out above, Le does not include a second cannula. Further, there is no motivation or suggestion to provide a second cannula. Rather, Le is specifically designed for insertion into and through lengthy vascular paths. Thus, a strain relief, which provides reinforcement in the catheter in the area where the user applies force on the catheter is advantageous. Further there is absolutely no motivation to modify the strain relief such that it would be located intraocularly (modification to move it almost 3-6 feet closer to the distal end of the catheter tube 16, or modification of the catheter tube by shortening it almost 3-6 feet in length). Rather, this would make the device unsuitable for its intended purpose because the catheter tube 16 would then be too short for insertion into and through vascular pathways (e.g. from the thigh to the heart) and/or it would be too stiff near its proximal tip (due to the reinforcement nature of the strain relief, which would now be located an inch or two from the proximal tip of the catheter tube)s.

Accordingly, claims 1-3 are patentable over Le. Claims 4, 12-16, 19, 21-23 and 25-33 depend from claims 1-3 and, likewise, are patentable over Le. Reconsideration and withdrawal of the rejection is respectfully requested.

Claims 5-7

Claims 5-7 have been rejected under 35 U.S.C. §103(a) as being unpatentable over Le in view of Weiss (US Pat#6,402,734). The Office asserts that:

> Le meets the claim limitations as stated above but fails to include the distal end being sharp and rigid with a bevel at about 30°.

> Weiss discloses an apparatus and method for cannulating retinal blood vessels. The device includes a microcannula with a beveled end (see figure 1).

Applicants respectfully traverse for the reasons set forth above regarding Le. Further, Weiss does not remedy the deficiencies of Le. Weiss, like Le, does not possess the flexibility of the cannula as set out by Applicants. Thus, claims 1-3 are patentable over Le in view of Weiss. Claims 5-7 depend from claims 1-3 and, likewise are patentable over Le in view of Weiss.

Further, there is no suggestion to modify Le to include a sharp, rigid distal end as set forth in Applicants' claim 5. Rather, there would be very strong reasons and motivation not to include such a distal end. As set forth above, the Weiss device is specifically designed and used for insertion into and through tortuous vascular pathways. Thus, the Weiss catheter is inserted into a vein, for example, and it pushed from its proximal end to advance the length of the catheter through the vein. Providing a sharp, rigid distal end could result in significant problems and drawbacks. The distal end of the catheter is the leading end of the device that makes its way first through the vein. As known and as stated in Weiss, such veins are tortuous and, thus, contain many bends and curves. As the catheter is pushed through the vein, the distal end will inevitably be pushed towards and into the walls of the vein, particularly at sharp bends. If the distal tip is sharp and rigid, then it will lodge itself into the walls, thereby preventing further advancement of the catheter through the vein. Even more problematic, a sharp, rigid distal tip could even be pushed through the wall of the vein resulting in a punctured vein.

Thus, there is no motivation to modify Le to include a rigid, sharp distal end. Rather, there is every motivation not to include such a distal end.

Thus, claim 5 is further patentable over Le in view of Weiss. Claims 6-7 depend from claim 5 and, likewise, are patentable over Le in view of Weiss.

Claim 24

Claim 24 has been rejected under 35 U.S.C. §103(a) as being unpatentable over Le in view of Weiss (US Pat#6,402,734). The Office asserts that:

> Le meets the claim limitations as stated above but fails to include the flexible cannula being illuminated for enhanced visibility.
>
> Weiss discloses an apparatus and method for cannulating retinal blood vessels. The device includes a fiber optic positioned parallel with the cannula for enhanced visibility during use (see figure 3).

Applicants respectfully traverse for the reasons set forth above regarding Le. Further, Weiss does not remedy the deficiencies of Le. Weiss, like Le, does not possess the flexibility of the cannula as set out by Applicants. Rather, Weiss utilizes an "elongated non-bendable, relatively rigid hollow body member." Thus, claims 1-3 are patentable over Le in view of Weiss. Claims 24 depends from claims 1-3 and, likewise are patentable over Le in view of Weiss.

Further, there would be no motivation to modify Le to have a cannula being illuminated for enhanced visibility. As set out above, the device of Le is designed for insertion into and through tortuous pathways. Thus, the catheter tip is inserted into the vein, for example a vein in the upper thigh, and the catheter is pushed from its proximal end upwards through the vein to a target location such as, for example, the heart. A user of the Le catheter does <u>not</u> see into the vein that the catheter is traveling through. Rather, the user simply pushes the device from its proximal end and the device makes its way through the vein. Thus, there is no reason to illuminate the catheter, which will not be seen by the user in any event.

Accordingly, claim 24 is patentable over Le in view of Weiss.

Claims 8-11 and 17-18

Claims 8-11 and 17-18 have been rejected under 35 U.S.C. §103(a) as being unpatentable over Le. The Office asserts that:

> Le meets the claim limitations as described above but fails to include the cannula being made from polyimide and having the flexible cannula and second cannula dimensions of claims 9-11 and 17-18.
>
> At the time of the invention it would have been obvious to make the cannula from a material such as polyimide since the catheter is

> disclosed as having flexible properties and it has been held to be within the general skill of a worker in the art to select a known material on the basis of its suitability for the intended use. The motivation for using a medical grade plastic such as a polyimide would have been in order to reduce the incidence of allergic reaction of the skin to contact with non-medical grade plastic materials.

Applicants respectfully traverse for the reasons set forth above regarding Le. As set out, Le does not possess the flexibility of the cannula as set out by Applicants. Thus, claims 1-3 are patentable over Le. Claims 8-11 and 17-18 depend from claims 1-3 and, likewise, are patentable over Le.

Claims 34-35

Claims 34-35 have been rejected under 35 U.S.C. §103(a) as being unpatentable over Le in view of Castora (US Pat#5,947,296). The Office asserts that:

> Le meets the claim limitations as described above but fails to include a kit including one or more of the catheters packed in sterile conditions.
>
> Castora discloses a catheter kit with multiple catheters packaged in one kit. See figures.

Applicants respectfully traverse for the reasons set forth above regarding Le. Further, Castora does not remedy the deficiencies of Le. Castora relates to multipack packages for containing medical implements in separate pouches packaged together in a continuous strip. Castora does not does not teach or suggest a catheter having the flexibility of the cannula as set out by Applicants. Thus, claims 1-3 are patentable over Le in view of Castora. Claims 34-35 depends from claims 1-3 and, likewise are patentable over Le in view of Castora.

2. Allowable Subject Matter

The Office indicates that claims 39-57 would be allowable if rewritten to overcome the rejection(s) under 35 U.S.C. §112, second paragraph, set forth in this Office action and the include all the limitations of the base claim and any intervening claims.

Applicants respectfully submit that there were no 35 U.S.C. §112, second paragraph rejection(s) in the October 17, 2003 Office action. However, in the previous Office action, the Office rejected a number of claims based on 35 U.S.C. §112, second paragraph. In particular, in the previous Office action, claims 1, 5-33 and 39-57 were rejected under 35 U.S.C. §112, second paragraph. The Office stated that:

> Claims 5, 8, 9, 12, 24, 25 and 39 recite the limitation "the flexible cannula" or "the cannula". There is insufficient antecedent basis for this limitation in claim 1 which fails to positively set forth a flexible cannula or any cannula.

Applicants, thus, amended the claims and amended claim 39 as follows:

> 39. A method for manual retinal vein catheterization comprising [using the microcatheter system of any one of claims 1 through 3 by] inserting [the] a microcatheter system [or cannula] within a retinal vein [in an eye] and infusing solution into the retinal vein, whereby the microcatheter system [or cannula] remains within the retinal vein without an external holding device.

Such that claim 39 now reads:

> 39. (Previously amended) A method for manual retinal vein catheterization comprising inserting a microcatheter system within a retinal vein and infusing solution into the retinal vein, whereby the microcatheter system remains within the retinal vein without an external holding device.

Applicants respectfully submit that rejections based on lack of antecedent basis in claim 39 have been remedied and, thus, the 35 U.S.C. §112, second paragraph, rejection has been overcome. Accordingly, claim 39 is believed to be allowable as well as dependent claims 40-57. Reconsideration and withdrawal of the rejection is respectfully requested.

CONCLUSION

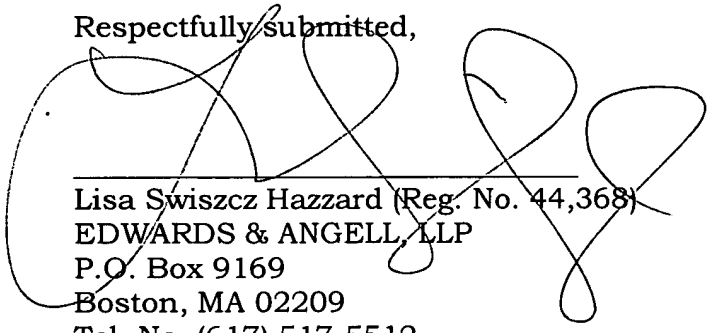
In light of the above amendments, Applicant respectfully requests early consideration and allowance of the subject application.

Applicants believe that additional fees are not required in connection with the consideration of the within matter. However, if for any reason a fee is required, a fee

paid is inadequate or credit is owed for any excess fee paid, you are hereby authorized and requested to charge Deposit Account No. **04-1105.**

Should the Examiner wish to discuss any of the amendments and/or remarks made herein, the undersigned attorney would appreciate the opportunity to do so.

Respectfully submitted,



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